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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,142	12/08/2000	Bernard Charles Sherman	PT-1877000	5119

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EXAMINER
DEWITTY, ROBERT M

ART UNIT	PAPER NUMBER
1616	9

DATE MAILED: 12/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/719,142	Applicant(s) SHERMAN, BERNARD CHARLES
	Examiner Robert M DeWitty	Art Unit 1616

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-11 are now pending in the instant application. Acknowledgement is made of Applicant's amendment and response filed 9/4/02.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

1. Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sims (Pat. No. 5,288,507), further in view of Stuerzebecher (Pat. No. 5,523,321) and Kararli et al. (Pat. No. 5,935,939).

Sims teaches compositions comprising a NSAID (ibuprofen)(col. 1, lines 51-53) and misoprostol (col. 4, lines 61-64). The composition may be administered in tablet form (col. 5, lines 1-3). Sims does not teach that NSAID and misoprostol are separately small tablets.

Kararli teaches that prostaglandins such as misorprostol are unstable and decompose above room temperature. Stablized amorphous dispersions of prostaglandins should be used in preparing pharmaceutical dosages. Kararli does not teach that NSAID and misoprostol are separately small tablets.

Stuerzebecher teaches the granulation of several components including prostaglandin and an antagonist that is then molded into round tablets. The amounts of prostaglandin and antagonist used are greatly reduced in comparison with the necessary dosages of the individual active substances.

It is the examiner's position that whereas Stuerzebecher does not term granules that make up the composition "tablets", granules are tablets of a specific size, and thus makes the use of "tablets" in the instant invention obvious. Motivation to utilize prostaglandin in combination with an NSAID such as ibuprofen would arisen in order to decrease the amount of prostaglandin and NSAID needed in comparison to taking the drugs separately. Furthermore, motivation to utilize a prostaglandin that has been dispersed in an excipient as taught by Kararli would have arisen in order to stabilize misoprostol used therein.

2. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franz et al. (Pat. No. 5,232,704), further in view of Stuerzebecher (Pat. No. 5,523,321).

Franz teaches a sustained release pharmaceutical dosage form comprised of a capsule including bi-layer formulation made of a release layer and a buoyant layer. The release layer may consist of a NSAID such as ibuprofen, and misoprostol. Amounts of components can be 25 to 75 mg for NSAID and 100-200mm for misoprostol (col. 4, lines 4-10). The ingredients can be contained in clear, hard gelatin capsules. Franz does not teach the ingredients are tablets.

Stuerzebecher teaches combination products containing a prostaglandin and an antagonist. The amounts of the ingredients are greatly reduced in comparison with the necessary dosages of individual active substances.

Stuerzebecher does not term the granules that make up the composition "tablets", however it the examiner's position that the granules are tablets of a specific

size. Motivation to make the bilayer of Franz in the form of Stuerzebecher would have arisen in order to greatly reduced the amounts of misoprostol and NSAID used, in comparison to the necessary dosages of the individual substances.

Response to Arguments

3. Applicant's arguments filed 9/10/02 have been fully considered but they are not persuasive.

4. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

With regards to Applicant's argument that the examiner has used 20/20 hindsight reasoning in combining the teachings of Sims, Kararli, and Stuerzebecher, and further

that the art does not teach the limitations of the amended claim, as shown with the definition provided by Applicant that granules are "small masses" (page 6 of Applicant's response) the examiner's position that such granules can be considered small tablets is further supported. Further, Applicant has defined "tableting", but has not defined a "tablet". A "tablet" is defined as "a small flat pellet of medication (see American Heritage Dictionary definition). A "pellet" is defined as "a small solid densely packed ball or mass" (Id.). Applicant has provided neither size nor dimensions for the small tablets used in the larger tablet. Sims clearly teaches the tableting of a composition that can contain an NSAID and misoprostol, and Stuerzebecher teaches a composition made of various granules (including antagonist and prostaglandin) and molded into tablet. The examiner's position is thus supported and the first rejection under 35 U.S.C. 103 is maintained.

Applicant asserts that in the second rejection under 103(a), Franz does not teach using two tablets contained within a pharmaceutical tablet including a shell which surrounds the two smaller tablets. However, Franz teaches a release layer consisting of an NSAID and a misoprostol, the final formulation containing a hard gelatin capsule. Franz does not teach that the ingredients are smaller tablets. Stuerzebecher teaches the production of granules, or "small masses" (Applicant's supplied definition), used to make a combination product. It is the examiner's position that such small masses or granules would be considered by one in the art as small tablets. Motivation to use the combination product of Stuerzebecher with Franz would have arisen to reduce the

amounts of misoprostol and NSAID used to make the formulation. As Franz teaches using a hard gelatin capsule, the granules, or small masses, would be contained within a shell. Thus the rejection is maintained.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M DeWitty whose telephone number is 703-308-2411. The examiner can normally be reached on 9:00am - 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose Dees can be reached on 703-308-4527. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7924 for regular communications and 703-308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

RMD
November 17, 2002

Alton N. Pryor
Primary Examiner
A.U. 1616